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Demonstration of Postvalvuloplasty Hemodynamic Improvement in Aortic Stenosis Based on Doppler Measurement of Valvular Resistance

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It was recently suggested that valvular resistance, defined as the pressure gradient/flow rate ratio, may better depict the hemodynamic impairment in aortic stenosis than does valve area. The relation between aortic valve resistance and left ventricular mechanics was studied with Doppler echocardiography in 13 patients (mean age 85 years) with severe aortic stenosis who underwent percutaneous balloon valvuloplasty.

The Doppler-estimated peak valvular resistance, defined as the ratio of peak transvalvular pressure gradient to peak valvular flow rate, decreased from 510 ± 190 dynes·s·cm^{-5} before valvuloplasty to 300 ± 110 dynes·s·cm^{-5} after the procedure ($p = 0.0001$). There was a close linear relation between valvular resistance measured at catheterization and Doppler-derived peak valvular resistance ($r = 0.91$). After valvuloplasty, left ventricular ejection fraction increased from 53 ± 13% to 62 ± 11% ($p = 0.0001$). The percent increase in ejection fraction was linearly related to the percent decrease in end-systolic wall stress ($r = 0.56$), which was in turn related to the percent decrease in peak valvular resistance ($r = 0.75$). No such linear relation existed between the percent changes in valve area and those in end-systolic wall stress.

In conclusion, hemodynamic improvement after valvuloplasty is more closely related to changes in valvular resistance than to changes in valvular area. It is suggested that valvular resistance can be estimated accurately by Doppler echocardiography with use of a simple method and should be a primary consideration in assessing the hemodynamics of aortic stenosis.

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Balloon aortic valvuloplasty has been proposed as an alternative treatment for patients with critical aortic stenosis who are high risk surgical candidates (1,2). Since these initial reports, most of the published studies (3–9) have focused on the clinical outcome of the procedure and have described the anatomic and hemodynamic changes after valvuloplasty in terms of valve area, transvalvular pressure gradient, cardiac output and ejection fraction. Most of the studies (3–9) have reported a significant improvement in left ventricular systolic pump function as assessed by cardiac output and ejection fraction after balloon aortic valvuloplasty. However, the mechanism by which ventricular pump function is improved after valvuloplasty has not been clarified. The changes in global left ventricular pump performance in an individual patient can be inferred from those in subvalvular peak velocity and mean acceleration (10). In a recent study, Ferguson et al. (11) evaluated the effects of balloon aortic valvuloplasty on ejection dynamics by analyzing the transstenotic jet waveform changes, but no data exist regarding the changes in the subvalvular flow pattern.

Because the pressure decrease across a stenosis is flow dependent, calculation of the valve area has been widely used to assess aortic stenosis, and valvuloplasty success is usually inferred from an increase in valve area. However, the relation between changes in valve area and hemodynamic improvement after balloon valvuloplasty has not been studied. Moreover, previous studies (12–16) have suggested that the anatomic valve area may also be a dynamic variable that is dependent on flow rate. Therefore, measurement of valve area may not be fully informative in assessing the results of balloon aortic valvuloplasty or in evaluating the hemodynamic impairment in aortic stenosis.

Use of the simple ratio of transvalvular pressure difference to flow rate as a stenotic index was proposed many years ago (17,18). This old concept was restored recently by Ford et al. (19), who proposed assessing the functional impairment in aortic stenosis by calculating the "resistance" that the stenotic valve opposes to blood flow based on the transvalvular pressure difference (ΔP) to flow rate (Q) ratio: Valvular resistance = ΔP/Q. Using catheter-derived data, the investigators (19) calculated valvular resistance as the mean transvalvular pressure difference (mean ΔP) to mean flow rate (mean Q) ratio. From the analysis of published

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studies, they showed that the calculated valve area changed at least three times more than resistance when the pressure gradient was varied. Because valvular resistance appeared to be less dependent on conditions of measurement than valve area, the investigators (19) suggested that valve resistance might be a better indication of hemodynamic obstruction.

The purpose of the present study was to 1) propose a simplified noninvasive method for calculating valvular resistance, and 2) to study the relation of valvular resistance and valve area to the hemodynamic impairment of aortic obstruction.

Methods

Study patients. Thirteen patients undergoing balloon valvuloplasty for critical aortic stenosis were evaluated. There were four men and nine women with a mean age of 85 ± 5 years (range 78 to 93). All patients were symptomatic, with either congestive heart failure, angina or a prior history of syncope. Patients were not considered candidates for valve replacement if they were of advanced age or had poor left ventricular function with end-stage heart failure or a significant associated medical disorder. Aortic root angiography and Doppler echocardiography showed no aortic regurgitation in five patients and trace to mild aortic regurgitation in eight. Left ventriculography and Doppler echocardiography showed no mitral regurgitation in 10 patients and mild mitral regurgitation in 3. No patient had a clinical history or electrocardiographic findings of past myocardial infarction. Four patients had coronary artery disease defined by coronary angiography as ≥ 50% luminal diameter narrowing of at least one major coronary artery (three-vessel disease in three patients and one-vessel disease in one patient). No patient had a regional wall motion abnormality on two-dimensional echocardiographic examination or ventriculography. All patients gave informed consent for balloon aortic valvuloplasty after they were informed of the potential risks and complications of the procedure.

Balloon valvuloplasty procedure and invasive measurements. All patients underwent retrograde percutaneous aortic valvuloplasty by means of the femoral artery. Balloon catheters (Mansfield Scientific) with 15- to 25-mm diameter balloons were used. A single balloon was used in nine patients (balloon diameter 18 mm in one patient, 20 mm in six patients and 25 mm in two patients). The double-balloon technique was used in four patients (balloon diameter 15 and 18 mm in one patient, 18 and 20 mm in two patients and 20 and 25 mm in one patient). In all patients, the transaortic pressure gradient was obtained by simultaneous measurement of left ventricular and ascending aorta pressures through fluid-filled catheters. Cardiac output was measured before and after valvuloplasty with either thermodilution or Fick output techniques.

According to the method described by Ford et al. (19), mean valvular resistance in dynes·s·cm^{-5} was calculated from catheterization data as: Mean valvular resistance = 1.333 × [Mean ΔP/Mean Q], where mean ΔP is the mean systolic pressure gradient in mm Hg and 1.333 is a factor that converts mm Hg to dynes/cm^2. Mean Q is the mean systolic flow rate in cm^3/s determined as follows: Mean Q = [1,000 × CO/60]/FET, where CO is the cardiac output (in liters/min) and FET is the fraction of the cardiac cycle during systole (that is, the ratio of systolic ejection period to duration of cardiac cycle).

Pre- and postvalvuloplasty ultrasound study. Noninvasive data were obtained with commercially available Doppler echocardiographic equipment and either 2.25- or 3.5-MHz transducers. Prevalvuloplasty ultrasound studies were performed ≤24 h (range 16 to 24, median 18) before valvuloplasty. Postvalvuloplasty ultrasound studies were performed ≤6 h (range 1 to 6 h, median 2) after the procedure. With use of orthogonal apical two- and four-chamber views, end-diastolic and end-systolic volumes were determined by means of measured areas and lengths using the method of discs, as recommended by the American Society of Echocardiography (20). The left ventricular outflow tract diameter was measured in the long-axis parasternal view just below the insertion of aortic valve leaflets as previously described (21,22). Diameters (d) were obtained between the two inner echocardiographic edges. Left ventricular outflow tract cross-sectional area was calculated as $\pi d^2/4$. Left ventricular end-diastolic and end-systolic minor-axis dimensions as well as wall thickness were measured from parasternal M-mode echocardiographic recordings acquired perpendicular to the left ventricular long axis and through the midline of short-axis two-dimensional images. Care was taken to record the largest left ventricular minor-axis dimensions present between the tips of the mitral valve leaflets and the superior aspect of the papillary muscles.

According to the recommendations of the American Society of Echocardiography, left ventricular internal dimension and wall thickness at end-diastole were measured at the onset of the QRS complex; left ventricular internal dimension at end-systole was measured at minimal internal dimension and end-systolic wall thickness was measured at maximal thickness. The transstenotic jet velocity was recorded by continuous wave Doppler recording from the apical, suprasternal or right sternal border, depending on where the highest and best quality velocity signal could be obtained. Subvalvular flow velocities were recorded from the apical window with pulsed wave Doppler recording. The sample volume was placed into the valve leaflets and gradually moved backward until the first clear ventricular outflow velocity was obtained.

Ultrasound data analysis. For subvalvular flow and jet velocity measurements, the recorded data from three cycles were digitized and analyzed off-line with use of a microcomputer interfaced with a videotape.

The peak subvalvular flow velocity and mean subvalvular acceleration, defined as the ratio of peak subvalvular velocity to the time to peak velocity, were measured.

The instantaneous transaortic valvular pressure gradient was calculated from the Doppler velocity using the simplified Bernoulli equation (Pressure gradient = 4 × [Velocity]^2). The maximal and mean pressure gradients were determined. Valve area was calculated from the continuity equation as previously validated (22,23). The Doppler mean valvular resistance (mean Rdop [dynes·s·cm^{-5}]) was calculated as follows: Mean Rdop = 1.333 × (Mean ΔP/Mean Q), where Mean ΔP (mm Hg) = Mean (4 × [Jet velocity]^2) and Mean Q (cm^3/s) = Outflow tract cross-sectional area (CSA) × Mean subvalvular velocity. *The Doppler-derived peak valvular resistance [peak Rdop [dynes·s·cm^{-5}]) was calculated as:* Peak Rdop = 1.333 × [ΔPmax/Qmax], where ΔPmax = 4 × (Peak jet velocity)^2 and Qmax = CSA × Peak subvalvular velocity.

Left ventricular meridional wall stress (σm) was calculated by using the angiographically validated formula of Grossman et al. (24): $\sigma m = 1.333 \cdot P \cdot D/4h(1 + h/D)$, where P = pressure (mm Hg), h = wall thickness (cm) and D = cavity minor dimension (cm). σm is expressed in 10^3·dynes/cm^2. End-systolic wall stress and wall stress at the time of peak subvalvular velocity were also determined.

For calculating the wall stress at the time of peak subvalvular flow velocity, the following timing method was used (Fig. 1). The time that peak subvalvular velocity occurred in the cardiac cycle and the ratio of the time to peak velocity to the ejection period were first determined with use of Doppler recording. The short-axis minor dimension and wall thickness at the time of peak subvalvular velocity were determined on the M-mode echocardiogram with use of time-matched cardiac cycles (Fig. 1). Left ventricular pressure at the time of peak subvalvular velocity was estimated from the time to peak subvalvular velocity/ejection period ratio; this ratio, calculated by Doppler recording, allowed determination of the left ventricular pressure at the time of subvalvular peak velocity when it was applied to the time interval between the two crossover points of left ventricular-aortic pressures (Fig. 1).

Left ventricular ejection fraction was calculated by biplane two-dimensional echocardiography (20) as the end-diastolic–end-systolic volume difference/end-diastolic volume ratio. End-systolic wall stress/end-systolic volume ratio, an index of contractility (25–27), was also calculated.

Statistical analysis. All values were expressed as mean values ± SD. Data were compared before and after aortic valvuloplasty for each patient using Student's paired *t* test. The correlation between mean valvular resistance determined by catheterization and Doppler-estimated resistances was obtained by using linear regression analysis. The correlation between the percent changes in subvalvular flow peak velocity, mean acceleration, wall stress at peak velocity and ejection fraction versus the percent changes in valve area and valvular resistance were determined with linear regression analysis. The relation between valve area and valvular resistance was analyzed by using the best fit curve. A p value < 0.05 was considered a significant difference.

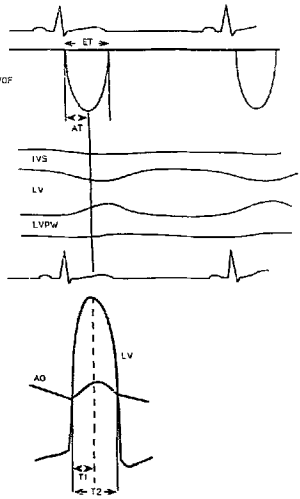

Figure 1. Method used to estimate left ventricular wall stress at the time of subvalvular peak flow velocity. The recording of subvalvular flow is represented schematically on the **upper panel**; with use of time-matched cycles, the left ventricular dimensions (cavity diameter and wall thickness) at the time of subvalvular peak velocity are determined on the M-mode echocardiogram (**middle panel**). The **lower panel** schematically represents the simultaneous recording of pressures in the proximal ascending aorta (AO) and in the left ventricle (LV). Left ventricular pressure at the time of subvalvular peak velocity is the pressure corresponding to the **vertical dashed line**; this **dashed line** is determined so that the ratio T1/T2 is equal to the ratio AT/ET, where AT = acceleration time or time to peak outflow velocity, ET = ejection time, T1 = the time interval between the first crossover point of left ventricular to aortic pressures and the left ventricular pressure at the time of subvalvular peak velocity, and T2 = time interval between the two crossover points of left ventricular to aortic pressures. IVS = interventricular septum; LVOF = left ventricular outflow; LVPW = left ventricular posterior wall.

Results

The balloon aortic valvuloplasty procedure was well tolerated in all 13 patients. There were no complications directly attributable to the balloon inflations and no clinical evidence of calcium embolic phenomena. Aortic regurgitation assessed by Doppler echocardiography and aortic root angiography was unchanged in 10 patients. Three patients who had no aortic regurgitation before the procedure devel-

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Table 1. Measurements Before and After Valvuloplasty in 13 Patients

	Before Valvuloplasty	After Valvuloplasty	p Value
Peak pressure gradient (mm Hg)	85 ± 23	60 ± 22	0.0001
Mean pressure gradient (mm Hg)	53 ± 17	37 ± 14	0.0001
Valve area (cm^2)	0.49 ± 0.12	0.70 ± 0.19	0.0301
Mean valvular resistance (dynes·s·cm^{-5})	461 ± 186	269 ± 96	0.0001
Peak valvular resistance (dynes·s·cm^{-5})	510 ± 190	300 ± 110	0.0001
Ejection fraction (%)	53 ± 13	62 ± 11	0.0001
Subvalvular peak velocity (cm/s)	83 ± 18	97 ± 18	0.004
Subvalvular mean acceleration (cm/s per s)	515 ± 124	767 ± 314	0.02
σm at subvalvular peak velocity (10^3·dynes/cm^2)	123 ± 28	99 ± 18	0.005
End-systolic σm (10^3 dynes/cm^2)	46 ± 15	40 ± 13	NS
End-systolic σm/end-systolic volume (10^3·dynes/cm^2 per ml)	1.39 ± 0.45	1.46 ± 0.59	NS

All data are expressed as mean values ± SD. σm = meridional wall stress.

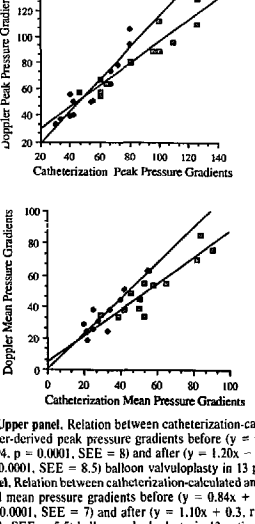


Figure 2. Upper panel. Relation between catheterization-calculated and Doppler-derived peak pressure gradients before (y = 0.84x + 12, r = 0.94, p = 0.0001, SEE = 8) and after (y = 1.20x − 5.8, r = 0.93, p = 0.0001, SEE = 8.5) balloon valvuloplasty in 13 patients. **Lower panel.** Relation between catheterization-calculated and Doppler-derived mean pressure gradients before (y = 0.84x + 4.3, r = 0.92, p = 0.0001, SEE = 7) and after (y = 1.10x + 0.3, r = 0.93, p = 0.0001, SEE = 5.5) balloon valvuloplasty in 13 patients. ◻ = before valvuloplasty; ◆ = after valvuloplasty.

oped trace to mild (n = 1) and moderate (n = 2) aortic regurgitatio' after balloon valvuloplasty.

Stenotic i dexes. The postvalvuloplasty changes in Doppler-derived t ansvalvular peak and mean pressure gradients, Doppler me. n and peak valvular resistance and valve area are shown in Table 1. In the 13 patients, there was a close linear correlation between Doppler and catheterization mean pressure grad'ents, as well as between Doppler and catheterization peak instantaneous pressure gradients, for both pre- and postvalvuloplasty studies (Fig. 2). There was also a high linear correlation between mean and peak valvular resistance determined by Doppler recordings as well as between catheterization mean valvular and Doppler resistance (Fig. 3).

Left ventricular mechanics (Table 1). The heart rate at echocardiographic examination was 88 ± 18 beats/min before and 91 ± 19 beats/min after valvuloplasty (p = NS). The heart rate at catheterization was 91 ± 18 beats/min before and 89 ± 17 beats/min after valvuloplasty (p = NS). There was no significant difference in the heart rate recorded at the time of ultrasound study and that recorded at the time of catheterization. Balloon valvuloplasty resulted in a significant increase in subvalvular peak flow velocity, mean subvalvular flow acceleration and ejection fraction. Systolic wall stress at peak subvalvular velocity also decreased significantly. This decrease in early systolic wall stress was due to a decrease in left ventricular pressure from 191 ± 35 to 153 ± 23 mm Hg (p = 0.0001), with no significant change in left ventricular cavity dimension (3.7 ± 0.6 vs. 3.6 ± 0.6 cm). End-systolic wall stress decreased by 13% after valvuloplasty, but this difference was not statistically significant. The end-systolic wall stress-end-systolic volume ratio was unchanged.

Relation of valve area and valvular resistance changes to hemodynamics (Fig. 4 to 7). Because the Doppler peak valvular resistance was closely and linearly related to Doppler mean resistance, the relation between hemodynamic changes and resistance changes was studied on the basis of peak resistance measure. ents. There was a significant linear relation between the percent changes in wall stress at the time of peak flow velocity and the percent changes in subvalvular peak velocity (r = 0.74, p = 0.004) and acceleration (r = 0.57, p = 0.04) (Fig. 4). Percent changes in wall stress at the time of peak velocity were in turn closely related to those in valvular resistance, with a correlation coefficient of r = 0.88 (Fig. 5). There was also a linear relation between the percent changes in valvular resistance and those in subvalvular peak velocity (r = 0.72, p = 0.005) and those in subvalvular acceleration (r = 0.65, p = 0.01). Percent changes in ejection fraction were linearly related to percent changes in end-systolic wall stress (r = 0.56, p =

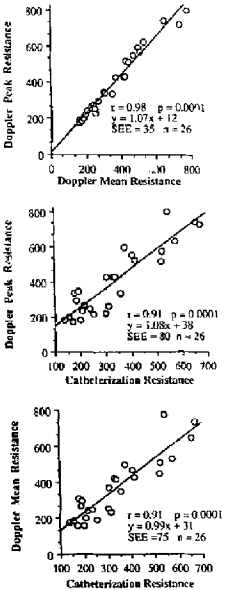


Figure 3. Relation between Doppler-derived values for peak and mean resistance **(top)**, Doppler-derived peak resistance and catheterization-calculated mean resistance **(middle)** and Doppler-derived mean resistance and catheterization-calculated mean resistance **(bottom)**. Resistance is expressed in dynes·s·cm^{-5}.

0.048), which were in turn linearly related to percent changes in valvular resistance ($r = 0.75$, $p = 0.001$) (Fig. 6). The percent changes in ejection fraction showed a trend of linear relation with valvular resistance percent changes ($r = 0.43$, $p = 0.14$). No significant linear relation was found between percent changes in valve area and those in ejection fraction ($r = 0.10$, $p = 0.74$), wall stress at peak velocity ($r = 0.06$), end-systolic wall stress ($r = 0.29$, $p = 0.34$), subvalvular peak velocity ($r = 0.48$, $p = 0.10$) and mean acceleration ($r = 0.36$, $p = 0.23$). When both pre- and postvalvuloplasty data were examined to provide a wide range of valve areas, we found an exponential inverse relation between valvular resistance and valve area in our study patients ($r = 0.84$) (Fig. 7).

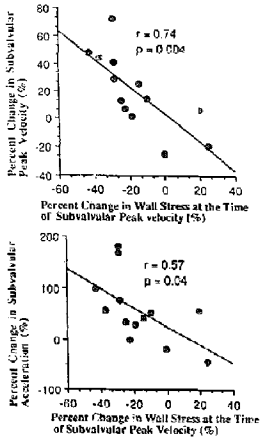
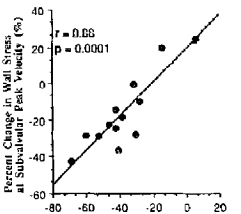


Figure 4. Relation of percent changes in subvalvular peak velocity (top) and mean acceleration (bottom) to percent changes in wall stress at peak subvalvular velocity.

Discussion

Noninvasive calculation of valvular resistance based on Doppler echocardiographic measurements. Our study demonstrates that valvular resistance in aortic stenosis, defined as the transvalvular pressure gradient/flow rate ratio (19), can be calculated noninvasively by Doppler echocardiography. In particular, the close correlation that we found

Figure 5. Relation between percent changes in wall stress at subvalvular peak velocity and percent changes in peak valvular resistance.



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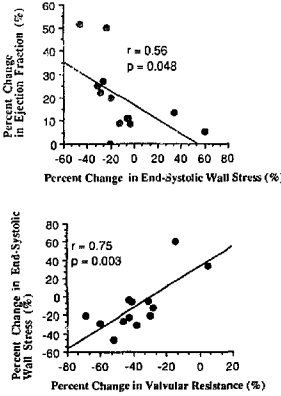
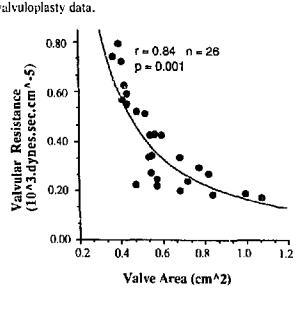


Figure 6. Relation of percent changes in ejection fraction (**top**) and end-systolic wall stress (**bottom**) to percent changes in peak valvular resistance.

between catheter-derived valvular resistance and Doppler-derived peak resistance suggests that valvular resistance can be estimated from a simplified ratio easily obtained by Doppler echocardiography.

Valvular resistance in aortic stenosis: a clinically useful but empiric tool or a theoretically justified index? The opposition to steady flow in a hydraulic conducting system is represented by resistance, which is expressed by a single number

Figure 7. Relation between Doppler-derived peak valvular resistance and valve area in the 13 study patients for pooled pre- and postvalvuloplasty data.



(that is, the ratio of pressure gradient to flow). However, because of the pulsatile characteristics of pressure and flow in the aorta, the arterial system is not only resistive, but also contains inertial and elastic components (28–30). Therefore, the total opposition to ventricular outflow is better described by the aortic *input impedance*, which represents the sum of the opposition due to inertial effects plus the opposition due to resistance and compliance (28–30). Impedance is computed as the complex ratio of a pressure harmonic to the flow harmonic at the same frequency using Fourier analysis (28,30). Experimental studies (30–34) have shown that input impedance influences left ventricular performance as assessed by peak ejection outflow rate, outflow acceleration and ejection fraction. Moreover it has been suggested (30–34) that impedance influences left ventricular performance through the wall stress. In a large channel like the proximal aorta with a normal aortic valve (insignificant valvular resistance), the inertial component of inpedance is dominant (28). However, in aortic stenosis, the impedance becomes essentially resistive because the resistance component is considerably increased as a result of the stenotic valve and the inertial component becomes proportionally less important (28). Therefore, valvular resistance is a hemodynamic characteristic that appears to be an appropriately descriptive term for assessing the opposition to the outflow in aortic stenosis.

Is valvular resistance calculated as the pressure gradient/flow rate ratio a hemodynamically stable index? The idea of assessing the degree of stenosis based on the transvalvular pressure gradient/flow rate ratio was suggested many years ago (17,18). However, the concept of valvular resistance was rejected by several investigators (13,35) on the theoretic grounds that resistance was less likely to remain constant at different flow rates than was calculated area. Ford et al. (19) recently showed on the basis of an analysis of five published studies that valve area calculated by the Gorlin formula changed at least three times more than did resistance when the pressure gradient was varied. Several investigators (36–38) subsequently confirmed the hemodynamic stability of valvular resistance. Martin et al. (36) studied the effects of submaximal exercise on indexes of valvular dysfunction in 78 patients with pure aortic stenosis. They (36) showed that the change in Gorlin-derived valve area (mean increase 13%) was significantly greater than the change in valvular resistance (mean decrease 4%). In 43 patients with aortic stenosis, Richard et al. (37) also showed that the percent change in valvular resistance is less than that noted in Gorlin-derived area during changes in flow and pressure induced by exercise (mean decrease 7% vs. a mean increase of 16%). In 11 patients with pure mitral stenosis, Beyer et al. (38) showed that after infusion of isoproterenol, mitral valvular resistance did not change, but Gorlin-derived valve area increased significantly.

Thus, all these published studies suggest that valvular resistance appears to be a hemodynamically stable index. In contrast, the Gorlin-calculated valve area appears to be

more affected by hemodynamic changes. The dependence of Gorlin-derived valve area on flow and pressure conditions may be attributed to the inclusion of an empiric constant in the Gorlin formula (12,39) and to variability in actual anatomic valve area (13–16). Gorlin's constant (K) is not a true constant because it incorporates two hydraulic coefficients: the discharge coefficient and the coefficient of orifice contraction, both of which vary with flow in stenotic valves (12,39). The continuity equation may be more accurate than the Gorlin formula for calculating valve area because it incorporates only one hydraulic factor, namely, the contraction coefficient (equation 2, Appendix) (39). However, even if more accurate than the Gorlin formula, calculation of valve area by the continuity equation may not be the reference standard for assessing the severity of a stenosis if there is significant variability in actual orifice area at different flow rates. A major advantage of resistance, calculated as the transvalvular pressure gradient/flow rate ratio, is that it does not require any assumptions as does the calculation of valve area. In this sense, valvular resistance may be a more useful index for clinical purposes than is calculated valve area.

From a purely physical point of view, is there any rationale for calculating valvular resistance in aortic stenosis as the simple transvalvular pressure gradient/flow rate ratio? Calculation of valvular resistance on the basis of simple transvalvular pressure gradient/flow rate ratio, a Poiseuille formula, implies a linear relation between flow (Q) and the first power of the pressure gradient: $Q = [1/R] \cdot \Delta P$. If one assumes resistance R to be constant, the pressure gradient (ΔP) is proportional to the first power of flow: $\Delta P = \text{Constant} \times Q$. Calculation of valve area with use of the Gorlin formula (35) implies a linear relation between flow (Q) and the square root of the pressure gradient: $Q = \text{Area} \cdot K\sqrt{\Delta P}$. If one assumes area and K (Gorlin's constant) to be constant, the pressure gradient (ΔP) must be proportional to the square of flow; $\Delta P = \text{Constant} \times Q^2$.

The area model and the resistance model cannot both be correct because the relation between flow and pressure gradient is different in the two models. In a *fixed obstruction*, it is obvious that pressure gradient is proportional to the square of flow as demonstrated by equation 6 in the Appendix. Indeed, in a fixed obstruction, the minimal anatomic area (As) is constant by definition and the contraction coefficient (Cc) remains relatively constant over a wide range of rates of flow as demonstrated previously (39). Thus, in a fixed obstruction, the pressure gradient is not proportional to the first power of flow and the resistance model is not valid from a strictly theoretic point of view. However, several studies (12–16) suggest that aortic stenosis cannot be considered a fixed obstruction because anatomic valve area increases with augmented flow rate. Segal et al. (39) also demonstrated that the contraction coefficient increases significantly with increasing flow rates for porcine stenotic valves.

Equation 8 in the Appendix shows that resistance is proportional to the first power of flow, but also is inversely proportional to the *squared product* of area with the contraction coefficient. Thus, even small changes in anatomic area and contraction coefficient result in magnified changes in the squared product of both terms and may contribute to maintain the resistance as constant despite augmented flow rate. Analysis of our data and review of previously published contraction coefficient data (39) reveal that the anatomic area would have to increase by only 9% (for example, from 0.58 to 0.63 cm^2) to maintain resistance as constant despite a 2.6-fold increase in flow rate (Appendix). Such flow-associated area changes are in agreement with previously published data (12,15,16). Thus, the changes in anatomic area and contraction coefficient may explain why resistance is maintained as constant despite changes in flow. This suggests that resistance might be a clinically valid and theoretically justified stenotic index for assessing valve obstruction.

Mechanism of improvement in systolic pump function after balloon valvuloplasty. Improvement in left ventricular systolic performance after balloon aortic valvuloplasty has been documented in previous studies (1–9). However, the mechanism by which left ventricular systolic pump function is improved has not been fully investigated. In a recent study, McKay et al. (4) suggested that theoretically an immediate improvement in systolic function could occur with an improvement in valve orifice area and the subsequent decrease in left ventricular afterload and systolic wall stress.

In agreement with previous reports (1–9), our study shows an improvement in global left ventricular systolic pump function after balloon valvuloplasty as demonstrated by an increase in subvalvular peak velocity, mean subvalvular flow acceleration and ejection fraction. The end-systolic wall stress/end-systolic volume ratio, an index of global contractility (25–27), was unchanged after valvuloplasty in our study. This observation is in agreement with the findings of Harpole et al. (7), who showed that contractility remains unchanged after balloon aortic valvuloplasty. In our patients, balloon valvuloplasty resulted in a significant decrease in wall stress at the time of peak subvalvular velocity. Percent increases in subvalvular peak velocity and mean acceleration were linearly related to percent decreases in the early systolic wall stress (that is, wall stress at the time of peak velocity), which were in turn linearly related to decreases in valvular resistance. Our results regarding the linear relation between changes in outflow acceleration and velocity and changes in early systolic wall stress are in agreement with the concept of a negative loading feedback that regulates the outflow ejection pattern (40). Percent increases in ejection fraction were linearly related to percent decreases in end-systolic wall stress, which were in turn linearly related to percent decreases in valvular resistance. No such linear relation existed between percent changes in valve area and those in end-systolic wall stress, wall stress at the time of peak velocity, subvalvular peak velocity, mean acceleration and ejection fraction. Thus, these findings sug-

gest that postvalvuloplasty hemodynamic improvement appears to be more closely related to changes in valvular resistance than to changes in valve area.

Clinical implications. Because of the high rate of restenosis reported recently in long-term follow-up studies (41), the indications for balloon aortic valvuloplasty probably will have to be more limited than was suggested in the earlier studies. However, this procedure offers the unique opportunity to assess the hemodynamic changes that occur after variable changes in valve area and consequently to better understand the pathophysiology of aortic stenosis. Our study shows that hemodynamic improvement after balloon aortic valvuloplasty is more related to changes in valvular resistance than to changes in valve area. This finding suggests that valvular resistance should be a primary consideration in assessing not only balloon aortic valvuloplasty, but also the hemodynamic impairment in aortic stenosis. Our results confirm the recent findings of Ford et al. (19), who suggested that valvular resistance may better depict the hemodynamic impairment of aortic obstruction than does valve area.

The relation between valvular resistance and valve area as demonstrated in Figure 7 is particularly informative. For extremely severe aortic stenosis (valve area <0.6 cm^2), only a small increase in valve area is associated with a large decrease in valvular resistance and significant hemodynamic improvement. Conversely, for less severe aortic stenosis (valve area >0.6 cm^2), a larger increase in valve area is necessary for a significant decrease in valvular resistance and significant hemodynamic improvement. This relation may explain why small increases in valve area have been reported to lead to major improvements in global ventricular function (2,4) and why postvalvuloplasty valve area alone does not seem to be a good predictor of clinical outcome (6).

Another potential advantage of measuring valvular resistance may be the usefulness of this index for assessing aortic obstruction in the presence of associated lesions such as aortic regurgitation, mitral regurgitation and ventricular dysfunction, all factors that influence ventricular ejection. Aortic regurgitation, by increasing forward flow, may affect the Gorlin formula-derived valve area as well as the actual anatomic area. For the same reasons, mitral regurgitation or ventricular dysfunction, by decreasing aortic forward flow, may also influence valve area measurements. In contrast, because valvular resistance has been shown to be less dependent on flow and pressure conditions than is the Gorlin formula-derived valve area, it should be less influenced by aortic regurgitation, mitral regurgitation and ventricular dysfunction.

Limitations of the study. It is possible that errors were introduced into our study by the use of nonsimultaneous measurement of invasive pressures and echocardiographic dimensions to calculate wall stress. Ultrasound data were recorded ≤24 h before and ≤6 h after valvuloplasty. However, the patients were in clinically stable condition before as well as after the procedure. In particular, the heart rate was the same at the time of ultrasound study and at catheterization. Furthermore, we found a good correlation between Doppler-derived pressure gradients and catheterization data. Thus, it is unlikely that significant changes in hemodynamics, particularly in left ventricular pressure, occurred during the interval between the invasive and noninvasive measurements. Furthermore, the relation we have described between percent changes in valve area and valvular resistance versus percent changes in subvalvular peak flow velocity, mean acceleration and ejection fraction were based only on ultrasound measurements. Therefore, the superiority of valvular resistance to valve area for assessing postvalvuloplasty hemodynamics in our study was not influenced by the time lag between invasive and noninvasive measurements.

The linear relation we found between percent changes in valvular resistance and those in subvalvular peak flow velocity may be artifactually enhanced because the equation for resistance depends on flow, which itself is calculated by measuring subvalvular velocity. However, if the relation between changes in resistance and in subvalvular flow velocity was only due to a mathematic artifact, one should expect the same significant relation between area and subvalvular velocity because subvalvular velocity is also included in the valve area calculation. Our results show that there was no significant linear relation between area changes and those in subvalvular velocity. Thus, the relation between percent changes in resistance and those in subvalvular velocity cannot be only a mathematic artifact. Similarly, the significant relation between valvular resistance and systolic wall stress changes could not be explained in this way.

Conclusion. This study shows that aortic valvular resistance defined as the transvalvular pressure gradient/flow rate ratio can be estimated accurately by Doppler echocardiography using a simplified method. The transvalvular pressure gradient/flow rate ratio represents an index of flow obstruction that appears to provide a better indication of hemodynamic impairment in aortic stenosis than does valve area.

Appendix

Definitions and Calculations

Definition of terms. A1 = inlet area (subvalvular area) (cm^2); A2 = vena contracta or jet area (cm^2); As = orifice minimal area (stenosis anatomic area) (cm^2); Cc = A2/As = contraction coefficient. Q = flow rate (cm^3/s); ΔP = pressure difference across the valve (mm Hg); V1 = velocity at inlet (subvalvular velocity) (cm/s); V2 = velocity at vena contracta (cm/s); ρ = mass density of blood (1.05 g/cm^3); μ = viscosity (dynes·s/cm^2); entry Reynolds number = $\rho V1D/\mu$, with D = inlet diameter.

Pressure gradient-flow relation across a stenosis. According to the Bernoulli equation:

$$\Delta P = 1/2\rho(V2^2 - V1^2). \quad [1]$$

According to the continuity equation, the flow rate Q can be written as:

$$Q = A1V1 = A2V2 = CcAsV2.$$

Thus,

$$V2 = Q/CcAs. \quad [2]$$

From equations 1 and 2, one obtains:

$$\Delta P = (1/2)\rho[Q^2/Cc^2As^2 - Q^2/A1^2]$$

$$= (1/2)\rho Q^2[1/Cc^2As^2 - 1/A1^2]. \quad [3]$$

Rearranging equation 3, one obtains:

$$Q = \sqrt{[(1/\rho)2\Delta P]} / [1/Cc^2As^2 - 1/A1^2]. \quad [4]$$

Equation 3 shows that the valvular resistance defined as the transvalvular pressure gradient-flow rate ratio can be written

$$R = \Delta P/Q$$

$$= (1/2)\rho Q[1/Cc^2As^2 - 1/A1^2]. \quad [5]$$

Assuming negligible preorifice velocity (V1) relative to jet velocity (V2) in equation 1, equation 3 reduces to:

$$\Delta P = (1/2)\rho Q^2[1/Cc^2As^2]. \quad [6]$$

Rearranging equation 6, one obtains

$$Q = \sqrt{[(1/\rho)2\Delta P]} / [1/Cc^2As^2] \quad [7]$$

and equation 5 becomes

$$R = (1/2)\rho Q[1/Cc^2As^2]. \quad [8]$$

If we consider As and Cc as constant, it is clear from equation 6 that the pressure gradient is proportional to the square of flow rate and equation 8 shows that resistance R varies linearly with the flow rate. Thus, if As and Cc are constant, as in a fixed obstruction, R is flow dependent. In contrast, R may remain constant if As and Cc vary with flow as in aortic stenosis. Equation 8 suggests that even small changes in As and Cc may be sufficient to maintain R constant because both terms are squared in the calculation of R.

Calculation of the extent to which area has to vary with flow to maintain resistance as constant. From equation 8:

$$As = [\sqrt{(1/2R)\rho Q}]/Cc. \quad [9]$$

In our study, the subvalvular peak flow velocity ranged from 49 to 129 cm/s. With a 1.9-cm outflow tract diameter (mean value in our study), these velocities result in calculated flow rates (Q) of 139 to 366 ml/s and entry Reynolds numbers of 2,819 to 7,423. These values for Reynolds numbers include the range in which Cc varies significantly for stenotic valves (39). Linear regression analysis of the entry Reynolds numbers and Cc data points published by Segal et al. (39) for a stenotic valve gives Cc = 0.63 for a 2,819 Reynolds number and Cc = 0.94 for a 7,423 Reynolds number. These findings and equation 9 show that for maintaining a constant valvular resistance R of 556 dynes·s·cm^{-5} (the value found in the patient with a 49-cm/s subvalvular velocity) despite a 2.6-fold increase in flow rate (from 139 to 366 ml/s), minimal anatomic area would have to increase from 0.58 to 0.63 cm^2. Such an extent in the flow-associated increase in anatomic valve area is in agreement with previously published studies (12,16). The same conditions also mean that area A2 calculated by the continuity equation (that is the product As·Cc: see equation 2) would increase from 0.37 to 0.59 cm^2.

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